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EXAMINER	
HUYNH, PHUONG N	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,674	MOSSALAYI ET AL.	
	Examiner	Art Unit	
	PHUONG HUYNH	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2009; 1/5/09*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-20,22-31,33,34,37-40,42-48,50,52-55 and 57-64* is/are pending in the application.

4a) Of the above claim(s) *15-20,22-31,33,34,37-39,42-48,50,52-55 and 57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,40 and 58-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *1/5/09* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 14-20, 22-31, 33-34, 37-40, 42-48, 50, 52-55 and 57-64 are pending.

2. Claims 15-20, 22-31, 33-34, 37-39, 42-48, 50, 52-55 and 57 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

3. Claims 14, 40 and 58-64, drawn to a compound comprising a CD23-binding peptide, an isolated polypeptide an amino acid sequence selected from the group consisting of SEQ ID NO: 1-10, an active fragment thereof, a peptidomimetic thereof other than retroinverted peptide thereof and cyclic peptide thereof, and a pharmaceutical composition comprising said peptide or polypeptide, are being acted upon in this Office Action.

4. The objection of claims 2-9, 38, 40 and 51 has been obviated by cancellation of said claims in amendments filed June 30, 2009 and January 5, 2009.

5. The objection to the disclosure under 37 CFR 1.821(d) has been obviated by the amendment June 30, 2009 and January 5, 2009.

6. The substitute declaration filed June 30, 2009 is acknowledged. Said declaration is acceptable.

7. The enablement and written description rejections of claims 1-13, 21, 32, 35-36, 40-41, 49, 51 and 56 under 35 U.S.C. 112, first paragraph has been obviated by the amendment June 30, 2009 and January 5, 2009.

8. The rejection of claims 1-3, 10-14, 21, 51 and 56 under 35 U.S.C. 102(b) as being anticipated by Jouault et al (Glycobiology 11 (8): 693-701,2001; PTO 1449) has been obviated by the claims amendment June 30, 2009 and January 5, 2009.

9. The rejection of claims 1, 7, 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jouault et al (Glycobiology 11 (8): 693-701,2001; PTO 1449) in view of US Pat No

5,028,592 (issued July 2, 1991; PTO 892) has been obviated by the claims amendment June 30, 2009 and January 5, 2009.

10. The rejection of claims 1, 35-36 and 40-41 under 35 U.S.C. 103(a) as being unpatentable over Jouault et al (Glycobiology 11(8): 693-701, 2001; PTO 1449) in view of Heck et al (Proc Natl Acad Sci 93:4036-4039, April 1996; PTO 892) has been obviated by the claims amendment June 30, 2009 and January 5, 2009.

11. The following new grounds of objections and rejections are necessitated by the amendment filed June 30, 2009.

12. Claim 61 is objected to because "said peptide *comprises an N-terminus* and wherein said N-terminus is acylated" is redundant since every peptide has an N-terminus and C-terminus. It is suggested that claim 61 be amended to recite "The composition according to claim 14 wherein the N-terminus of said peptide is acylated."

13. Claim 62 is objected to because it is unclear what is being acetylated. It is suggested that claim 62 be amended to recite "The composition according to claim 61 wherein the N-terminus of said peptide is acetylated."

14. Claim 14 is objected to because of typographical error "NH_2 Grally-]NWG[allyl-]" should have been "NH_2 G[ally-]NWG[allyl-]".

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

16. Claim 63 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The "said C-terminus" in claim 63 has no antecedent basis in base claim 14 because the word "C-terminus" is not recited in claim 14. It is suggested that claim 63 be amended to recite "The composition according to claim 14 wherein the C-terminus of said peptide is amidated."

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 14, 40 and 58-64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) an isolated CD23 binding peptide consisting of the amino acid sequence selected from the group consisting of SEQ ID NO: 1-10, (2) the said isolated peptide wherein the N-terminus of the peptide is acylated or the C-terminus of the peptide is amidated, (3) the said isolated peptide wherein the peptide is labeled for detection assays, (4) the isolated CD23 binding peptide consisting of the amino acid sequence selected from the group consisting of SEQ ID NO: 1-10 wherein at least one amino acid within said peptide is a D-isomer, (5) An isolated CD23 binding peptide consisting of the amino acid sequence of SEQ ID NO: 1 for treating rheumatoid arthritis by inhibiting Nitric oxide production and TNF production, **does not** reasonably provide enablement for any peptide "comprises" the amino acid sequence of any one of SEQ ID NO: 2 to 10, 31, 32, 34, 35, 40, 43 and 53-61 as set forth in claims 59-60 and 64, and any pharmaceutical composition comprising such peptide as set forth in claims 14, 58, and 61-63 for treatment or *prophylaxis* (prevention) of any disease or any disorder related to CD23 such as any autoimmune diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

Enablement is not commensurate in scope with how to make and use any polypeptide longer than the sequence set forth claim 59. The term "comprises" is open-ended. It expands the peptide to include additional amino acids at either or both ends. There is insufficient guidance as to what amino acids to be added such that the resulting peptide still binds specifically to CD23.

The specification discloses only peptide consisting of six or seven amino acid residues in length selected from the group consisting of SEQ ID NO: 1-10 or the specific peptide listed in Table I and II that inhibits the binding of monoclonal CD23 antibody to CD23 expressing cell *in vitro*. The specification discloses the N-terminus of the peptide HENWPS (SEQ ID NO: 7) is acylated or the C-terminus of the peptide is amidated. The specification discloses only one retroinverted peptide from HENWPS (SEQ ID NO: 7), which is SPWNEH. However, only the specific peptides of SEQ ID NO: 1-7 inhibit iNOS production as shown in Table 2. The specification further discloses administering only peptide FHENWPS (p30A) of SEQ ID NO: 1 inhibited the production of TNF and ameliorated the arthritis symptoms in in-bred Lewis rat induced mycobacterium butyricum (an adjuvant induced model of arthritis).

Even if the peptide is exact length, there is insufficient guidance and lack of *in vivo* working example such pharmaceutical composition comprising any one of the peptide set forth in claim 14 can treat any autoimmune diseases, let alone prevention (prophylaxis) of all autoimmune diseases.

It is well known in the art that the amino acid sequence of a protein determines the protein's structural and functional properties. Predictability of which changes can be tolerated in a protein's amino acid sequence to obtain a desired biological activity requires knowledge and guidance regarding specific amino acid residue(s) in the protein's amino acid sequence, if any, are tolerant of modification and which are conserved (i.e., expectedly intolerant to modification) and detailed knowledge of the protein's structure, and the ways in which the protein's structure relates to its function.

Stryer et al (of record, in Biochemistry, Third edition, W H Freeman Company, New York, pages 31-33, 1998; PTO 892). teach that a protein is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformational of the protein (See enclosed appropriate pages).

The positions within a protein's amino acid sequence where modifications can be made with a reasonable expectation of success in obtaining a protein having the same biological activity are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g., multiple substitutions, deletions, additions, and combinations thereof.

Ngo et al (of record, The Protein Folding Problem and Tertiary Structure Prediction, pp. 491-495, 1994; PTO 892) teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Methods for isolating or generating variants and mutants using random mutagenesis techniques were known in the art. However, neither the specification nor the state of the art at the time of the invention provided the necessary guidance for altering the protein comprising an amino acid sequence of SEQ ID NO: 1 with an expectation of obtaining a derivative maintaining the same biological activity.

At the time of the invention, there was a high level of unpredictability associated with altering a protein sequence with an expectation that the protein will maintain the same desired biological activity. For example, the specification discloses substituting even a single amino acid in the peptide of SEQ ID NO: 1 from P to A resulted in lost of inhibition of iNOS production from 74% to 26%, see specification at page 28, Table II compound 328, in particular.

With respect the pharmaceutical composition comprising any peptide other than SEQ ID NO: 1, the specification discloses administering only one peptide (p30A) consisting of the amino acid sequence FHENWPS (SEQ ID NO: 1) that inhibited the production of TNF and ameliorated the arthritis symptoms in in-bred Lewis rat induced mycobacterium butyricum (adjuvant induced model of arthritis).

However, the specification does not disclose administering any peptide sequence as set forth claim 14 other than SEQ ID NO: 1 is effective for treating any autoimmune diseases or preventing any autoimmune diseases other than SEQ ID NO: 1 for inhibiting the production of TNF and ameliorates arthritis.

Given the enormous number of peptides and autoimmune diseases, there is insufficient *in vivo* working example to show administering one species of peptide (SEQ ID NO: 1) is predictable of treating and preventing all diseases, especially all autoimmune diseases.

Van Noort et al (of record, International Review of Cytology 178: 127-205, 1998; PTO 892) teach autoimmune diseases can be species and model-dependent (See entire document, pages 167-168, in particular).

Since the therapeutic indices and structure of the peptide longer than the specified SEQ ID NO has can described, and the autoimmune diseases can be species- and model-dependent, it

is not clear that reliance on the use of adjuvant induced arthritis rat model with one peptide consisting with SEQ ID NO: 1 accurately reflects the relative efficacy of treating all diseases by administering any peptide, much less preventing any and all autoimmune diseases.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed June 30, 2009 and January 5, 2009 have been fully considered but are not found persuasive.

Applicants' position is that the claims have been amended to recite peptide sequences which have been synthesized and/or tested and described in the present application, i.e., SEQ ID NOs 1-10, 31, 32, 34, 35, 40, 43 and 53-61 (Sequence listing and Tables I and II).

In response, the term "comprising" in claim 59 is open-ended ends. It expands the claimed peptide to include additional amino acids at either or both ends. There is a lack of guidance as to what amino acids to be added such that the resulting peptide still maintains its structure and function, i.e., binding to any CD23.

With respect the pharmaceutical composition comprising any peptide other than SEQ ID NO: 1, the specification discloses administering only one peptide (p30A) consisting of the amino acid sequence FHENWPS (SEQ ID NO: 1) that inhibited the production of TNF and ameliorated the arthritis symptoms in in-bred Lewis rat induced mycobacterium butyricum (adjuvant induced model of arthritis).

However, the specification does not disclose administering any peptide sequence as set forth claim 14 for treating any autoimmune diseases or preventing any autoimmune diseases other than SEQ ID NO: 1 for inhibiting the production of TNF and ameliorates arthritis.

Note, amending claim 14 to recite a composition rather than a pharmaceutical composition would obviate this rejection. Further, amending the term "comprises" in claim 59 to

"consisting of" and amending the preamble of claim 64 "A labeled peptide of claim 59" would obviate this rejection.

19. Claims 59-60 and 64 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 59 encompasses a genus of peptide comprises the amino acid sequence longer than the peptide set forth in SEQ ID NO: 2 to 10, 31, 32, 34, 35, 40, 43 and 53-61.

The scope of the each genus includes many members with widely differing structural, chemical, and physiochemical properties such as widely differing chemical groups, or amino acid sequences. Furthermore, each genus is highly variable because a significant number of structural and biological differences between genus members exist.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., complete or partial structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, method of making the claimed invention, level of skill and knowledge in the art and predictability in the art sufficient to show that applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provides only the bovine sequence.

In this case, the specification does not reasonably provide a **written description** for a genus of peptide mentioned above that is longer than 7 amino acid residues for treating or preventing any diseases, any disease such as any and all autoimmune diseases, any diseases such as cancer.

At the time of filing, the specification discloses only peptide consisting of six or seven amino acid residues in length selected from the group consisting of SEQ ID NO: 1-10 or the specific peptide listed in Table I and II that inhibits the binding of monoclonal CD23 antibody to CD23 expressing cell *in vitro* or inhibits iNOS production. The specification discloses the N-terminus of the peptide HENWPS (SEQ ID NO: 7) is acylated or the C-terminus of the peptide is amidated. The specification discloses only one retroinverted peptide of HENWPS, which is SPWNEH. However, only the non-retroinverted peptides of SEQ ID NO: 1-7 inhibits iNOS production as shown in Table 2. The specification further discloses administering peptide FHENWPS (p30A) of SEQ ID NO: 1 inhibited the production of TNF and ameliorated the arthritis symptoms in in-bred Lewis rat induced mycobacterium butyricum (adjuvant induced model of arthritis).

As of the filing date of instant application, Applicants are not in possession of any peptide "comprises" the amino acid sequence set forth in claim 59. There is not a single peptide that is longer than 7 amino acids residues in the specification as filed. The term "comprises" is open-end. It expands the peptide to include additional amino acids at either or both ends. There is a lack of disclosure as to what amino acids to be added to either or both ends such that the peptide still maintains binding to CD23.

Stryer et al (of record, in Biochemistry, Third edition, W H Freeman Company, New York, pages 31-33, 1998; PTO 892). teach that a protein is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformational of the protein (See enclosed appropriate pages). As such, the structure of claimed peptide is not adequately described.

Ngo et al (The Protein Folding Problem and Tertiary Structure Prediction, pp. 491-495, 1994; PTO 892) teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Methods for isolating or generating variants and mutants using random mutagenesis techniques were known in the art. However, neither the specification nor the state of the art at the time of the invention provided the necessary guidance for altering the protein comprising an amino acid sequence of SEQ ID NO: 1 with an expectation of obtaining a derivative maintaining the same biological activity.

At the time of the invention, there was a high level of unpredictability associated with altering a protein sequence with an expectation that the protein will maintain the same desired biological activity. For example, the specification discloses substituting even a single amino acid in the peptide of SEQ ID NO: 1 from P to A resulted in lost of inhibition of iNOS production from 74% to 26%, see specification at page 28, Table II compound 328, in particular.

Because the described peptides is not representative of the entire claimed genus, and the specification does not disclose structural features shared by members of the genus, one of skill in the art would conclude that applicant was not in procession of the claimed genus as a whole at the time of filing. Therefore, the specification fails to satisfy the written description requirement of 35 U.S.C. 112, first paragraph, with respect to the full scope of claims 59-60 and 64.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115). Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001 and revision of the Written Description Training materials, posed April 11, 2008 http://www.USPTO.gov/web/menu/written.pdf.

Applicants' arguments filed June 30, 2009 and January 5, 2009 have been fully considered but are not found persuasive.

Applicants' position is that the claims have been amended to recite peptide sequences which have been synthesized and/or tested and described in the present application, i.e., SEQ ID NOs 1-10, 31, 32, 34, 35, 40, 43 and 53-61 (Sequence listing and Tables I and II).

In response, there is not a single peptide that is longer than 7 amino acids residues in the specification as filed. The term "comprises" is open-end. It expands the peptide to include additional amino acids at either or both ends. There is a lack of disclosure as to what amino acids to be added to either or both ends such that the peptide still maintains binding to CD23. Because the described peptides is not representative of the entire claimed genus, and the specification does

not disclose structural features shared by members of the genus, one of skill in the art would conclude that applicant was not in procession of the claimed genus as a whole at the time of filing. Therefore, the specification fails to satisfy the written description requirement of 35 U.S.C. 112, first paragraph, with respect to the full scope of claims 59-60 and 64.

Note, amending claim 59 to recite "A CD23-binding peptide wherein said peptide *consisting of* the amino acid sequence of any one of SEQ ID NO: 2 to 10, 31, 32, 34, 35, 40, 43, and 53-61 would obviate this rejection. Further, it is suggested that claim 64 be amended to recite "A labeled peptide of claim 59 wherein said peptide is labeled with a detectable marker."

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

21. Claim 59 is rejected under 35 U.S.C. 102(b) as being anticipated by Jouault et al (of record, Glycobiology 11(8): 693-701, 2001; PTO 1449).

Jouault et al teach a FHENWPS which is 100% identical to the claimed SEQ ID NO: 1 wherein the reference peptide is coupled to KLH (see page 695, col. 1, page 696, Table 1, page 699, col. 2, first full paragraph, in particular). The reference peptide FHENWPS has identical amino acids to the claimed CD23-binding peptide FHENWP of SEQ ID NO: 1 or p30A in Table 2. The term "comprises" is open-ended. It expands the claimed peptide Phe-His-Glu-Asn-Trp-Pro (FHENWP) of SEQ ID NO: 4 or the claimed peptide His-Glu-Asn-Trp-Pro-Ser (HENWPS) of SEQ ID NO: 7 to include additional amino acid at either end, including KLH to read on the reference peptide. The reference peptide inherently binds to CD23 because the peptide has the same amino acid sequence. Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed June 30, 2009 and January 5, 2009 have been fully considered but are not found persuasive.

Applicants' position is that as now claimed there is provides a pharmaceutical composition comprising at least one CD23-binding peptide, wherein the peptide is selected from those now specifically listed in claim 14. The claimed pharmaceutical compositions as now claimed are not disclosed by Jouault. Jouault describes a peptide FHENWPS (having a sequence of SEQ ID NO: 1) that mimics J3-1,2-1inked mannoside from phosphopeptidomannane (PPM) of Candida albicans. Jouault uses the FHENWPS peptide as a mimotope which is recognized specifically by anti-1-l,2-1inked mannoside antibodies. Jouault also describes anti-FHENWPS antibodies recognizing the Saccharomyces cerevisiae PPM. However, Jouault contains no disclosure regarding pharmacological activity the FHENWPS peptide, and Jouault makes no mention of any capacity of the FHENWPS peptide to bind CD23 molecule. Jouault clearly does not anticipate the invention as now claimed.

The argument with respect to pharmaceutical composition is moot since the rejection of claims that are drawn to pharmaceutical composition has been withdrawn. However, the term "comprises" is open-ended. It expands the claimed peptide Phe-His-Glu-Asn-Trp-Pro (FHENWP) of SEQ ID NO: 4 or the claimed peptide His-Glu-Asn-Trp-Pro-Ser (HENWPS) of SEQ ID NO: 7 to include additional amino acid at either end, including KLH to read on the reference peptide. The reference peptide inherently binds to CD23 because the peptide has the same amino acid sequence. Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Thus, the reference teachings anticipate the claimed invention.

22. Claims 14, 40 and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by DE19749277 A1 (published May 5, 1999; PTO 1449).

The DE19749277 patent teaches a pharmaceutical composition comprising a peptide consisting of the amino acid sequence of FHENWPS and a pharmaceutical acceptable carrier such as PBS (see col. 2, lines 24-33, sequence, claim 4 of the patent, in particular). The reference peptide FHENWPS is 100% identical to the claimed peptide of SEQ ID NO: 1. The reference peptide FHENWPS inherently binds to CD23 such as at least about 10^{-6}M. Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and

its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure or sequence, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

Claim 59 is included in this rejection because the term "comprises" is open-ended. It expands the claimed peptide Phe-His-Glu-Asn-Trp-Pro (FHENWP) of SEQ ID NO: 4 or the claimed peptide His-Glu-Asn-Trp-Pro-Ser (HENWPS) of SEQ ID NO: 7 to include additional amino acid to read on the reference peptide. Furthermore the reference peptide FHENWPS anticipates the claimed peptide sequence FHENWXaaS of SEQ ID NO: 43 where Xaa is Ser. The reference peptide FHENWPS comprises the claimed peptide HENWXaaS of SEQ ID NO: 32 wherein Xaa is Pro. The reference peptide FHENWPS comprises the claimed peptide FHENWXaaS of SEQ ID NO: 43 where the Xaa is Pro. Thus, the reference teachings anticipate the claimed invention.

23. Claim 59 is rejected under 35 U.S.C. 102(b) as being anticipated by JP2002187899 (published July 5, 2002 PTO 1449).

JP2002187899 patent teaches a peptide such as Phe-His-Glu-Asn-Trp-Pro-Ser which is 100% identical to the claimed SEQ ID NO: 1 and is relevant to the structure of the claimed invention claimed in the instant application (see pages 2-5, reference SEQ ID NO: 5, in particular). The reference peptide comprises the claimed peptide (FHENWP) of SEQ ID NO: 4 and (HENWPS) of SEQ ID NO: 7 because the term "comprising" is open-ended. It expands the claimed peptide to include additional amino acid residues at either or both ends. Thus, the reference teachings anticipate the claimed invention.

24. Claim 59 is rejected under 35 U.S.C. 102(b) as being anticipated by Santamaria et al (Clinical Immunology 101(3): 296-302, 2001; PTO 892).

Santamaria et al (Clinical Immunology 101(3): 296-302, 2001 teaches a peptide such as Phe-His-Glu-Asn-Trp-Pro-Ser (FHENWPS) which is 100% identical to the claimed SEQ ID NO: 1 and is relevant to the structure of the claimed invention claimed in the instant application, see page 298, col. 2, in particular. The reference peptide comprises the claimed peptide (FHENWP) of SEQ ID NO: 4 and (HENWPS) of SEQ ID NO: 7 because the term "comprising" is open-

ended. It expands the claimed peptide to include additional amino acid residues at either or both ends. Thus, the reference teachings anticipate the claimed invention.

25. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

26. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

27. Claims 14 and 59-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jouault et al (Glycobiology 11(8): 693-701, 2001; PTO 1449) or DE19749277 A1 (published May 5, 1999; PTO 1449) or JP2002187899 (published July 5, 2002 PTO 1449) or Santamaria et al (Clinical Immunology 101(3): 296-302, 2001; PTO 892) each in view of US Pat No 5,028,592 (of record, issued July 2, 1991; PTO 892).

The teachings of Jouault et al, DE19749277 A1, JP2002187899 and Santamaria et al have been discussed supra. Jouault et al further teaches the peptide is useful for making antibody.

The invention in claims 60 and 62 differs from the teachings of the references only in that the peptide wherein the N-terminus is acylated.

The invention in claims 60 and 62 differs from the teachings of the references only in that the peptide wherein the N-terminus is acetylated.

The invention in claims 60 and 63 differs from the teachings of the references only in that the peptide wherein the C-terminus is amidated.

The '592 patent teaches protective groups such as acyl or acetyl group bound to the amino terminus or the amidated group to the C-terminus of any bioactive peptide to reduce the susceptibility of the peptide to acid or enzymatic hydrolysis (see col. 4, lines 50-66, in particular). The '592 patent teaches protected peptides are more active pharmacologically than the unprotected peptide (see col. 4, lines 65-66, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include a protective group such as acyl or acetyl group bound to the amino terminus or the amidated group to the C-terminus of any peptide as taught by the '592 patent to any one of the peptide comprises the amino acid sequence FHENWPS as taught by Jouault et al, or the FHENWPS peptide as taught by the DE19749277 A1 or the JP2002187899 patent or Santamaria et al.

One having ordinary skill in the art would have been motivated to do so because the protective groups would reduce susceptibility of the peptide to acid or enzymatic hydrolysis and the protected peptides are more active pharmacologically than the unprotected peptide as taught by the '592 patent (see col. 4, lines 50-66, in particular). Jouault et al further teaches the peptide is useful for making antibody. One having ordinary skill in the art would have been motivated to use known technique to improve peptide known in the art as taught by the '592 patent to improve the peptide from enzymatic hydrolysis as taught by Jouault et al. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Given the examination guidelines for determining obviousness under 35 U.S.C. 103 in view of the Supreme Court decision in *KSR International Co. V. Teleflex Inc. 82 USPQ2d 1385 (2007)* and the Examination Guidelines set forth in the Federal Register (Vol. 72, No. 195, October 10, 2007) and incorporated recently into the MPEP (Revision 6, September 2007), the following rationales to support rejection under 35 U.S.C. 103(a) are noted:

A) Combining prior art elements according known methods to yield predictable results.

B) Use of known technique to improve similar products in the same way.

C) "Obvious to try" --- choosing form a finite number of identified, predictable solutions, with a reasonable expectation of success.

D) Some teachings, suggestion, or motivation in the prior art that would lead to one of ordinary skill to modify the prior art reference to arrive at the claimed invention.

Since reducing enzymatic hydrolysis or peptide in vivo is desirable and have been predictable at the time the invention was made, there would have been reasonable expectation of success in combine the references teachings to arrive at the claimed invention. An obviousness is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See *KSR International Co. V. Teleflex Inc. 82 USPQ2d 1385 (2007).* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Applicants' arguments filed June 30, 2009 and January 5, 2009 have been fully considered but are not found persuasive.

Applicants' position is that Jouault contains no disclosure or suggestion of any pharmacological activity or CD23-binding activity of the FHENWPS peptide. Heck fails to cure this deficiency of Jouault. Heck describes treatment of inflammation by administering to an individual a pharmaceutical composition comprising a tripeptide Lys-Pro-Val, acylated at its amino terminus or amidated at its carboxy terminus. Heck is thus irrelevant to the invention as now claimed, since the peptide Lys-Pro-Val is unrelated to the presently claimed invention. The combined disclosures of Jouault and Heck would not have led one of ordinary skill to envisage the binding affinities of the disclosed peptides for CD23 molecule.

In response, Jouault discloses FHENWPS peptide having the same structure as that of claimed SEQ ID NO: 1; the reference peptide FHENWPS comprises the sequence of the claimed FHENWP of SEQ ID NO: 4 or the claimed peptide HENWPS of SEQ ID NO: 7. As explained earlier, products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure or sequence, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. As such, the intrinsically property of the claimed peptide such as CD23-binding activity as now claimed must present.

The invention in claims 60 and 62 differs from the teachings of the references only in that the peptide wherein the N-terminus is acylated.

The invention in claims 60 and 62 differs from the teachings of the references only in that the peptide wherein the N-terminus is acetylated.

The invention in claims 60 and 63 differs from the teachings of the references only in that the peptide wherein the C-terminus is amidated.

The '592 patent teaches protective groups such as acyl or acetyl group bound to the amino terminus or the amidated group to the C-terminus of any bioactive peptide to reduce the susceptibility of the peptide to acid or enzymatic hydrolysis (see col. 4, lines 50-66, in particular). The '592 patent teaches protected peptides are more active pharmacologically than the unprotected peptide (see col. 4, lines 65-66, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the protective groups such as acyl or acetyl group bound to the amino terminus or the amidated group to the C-terminus of any peptide of the '592 patent to any one of the peptide comprises the amino acid sequence FHENWPS as taught by Jouault et al or the DE19749277 A1 or the JP2002187899 patent or Santamaria et al.

One having ordinary skill in the art would have been motivated to do so because the protective groups would reduce susceptibility of the peptide to acid or enzymatic hydrolysis and the protected peptides are more active pharmacologically than the unprotected peptide as taught by the '592 patent (see col. 4, lines 50-66, in particular). One having ordinary skill in the art would have been motivated to use known technique of the '592 patent to improve a known peptide as taught by Jouault et al or DE19749277 A1 or the JP2002187899 patent or Santamaria et al to minimize the peptide from enzymatic hydrolysis or degradation as taught by the '592 patent.

28. Claims 14 and 58-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jouault et al (of record, Glycobiology 11(8): 693-701, 2001; PTO 1449) or DE19749277 A1 (of record, published May 5, 1999; PTO 1449) or JP2002187899 (of record, published July 5, 2002 PTO 1449) or Santamaria et al (of record, Clinical Immunology 101(3): 296-302, 2001; PTO 892) each in view of Heck et al (of record, Proc Natl Acad Sci 93:4036-4039, April 1996; PTO 892).

The teachings of Jouault et al, DE19749277 A1, JP2002187899 and Santamaria et al have been discussed supra.

The invention in claims 58 and 60 differs from the teachings of the references only in that the peptide has at least one amino acid which is a D-isomer instead of naturally occurring L-isomer.

Heck et al teach in recent years, a growing number of synthetic peptides containing D-amino acids to capitalize on the residues' ability to provide improved protease stability (pharmacokinetic profile) of the bioactive peptides (see page 4039, col. 2, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to improve the stability of the peptide of Jouault et al by substituting the natural occurring L-amino acid in the peptide of Jouault et al for the D-amino acid isomer as taught by Heck et al.

One having ordinary skill in the art would have been motivated to do so because Heck et al teach it is conventional at the time the invention was made to synthesize peptides containing D-amino acids to capitalize on the residues' ability to provide improved protease stability (pharmacokinetic profile), alter tertiary structure and affect activity of the bioactive peptides (see page 4039, col. 2, in particular).

Applicants' arguments filed June 30, 2009 and January 5, 2009 have been fully considered but are not found persuasive.

Applicants' position is that Jouault contains no disclosure or suggestion of any pharmacological activity or CD23-binding activity of the FHENWPS peptide. Heck fails to cure this deficiency of Jouault. Heck describes treatment of inflammation by administering to an individual a pharmaceutical composition comprising a tripeptide Lys-Pro-Val, acylated at its amino terminus or amidated at its carboxy terminus. Heck is thus irrelevant to the invention as now claimed, since the peptide Lys-Pro-Val is unrelated to the presently claimed invention. The combined disclosures of Jouault and Heck would not have led one of ordinary skill to envisage the binding affinities of the disclosed peptides for CD23 molecule.

In response, Jouault discloses FHENWPS peptide having the same structure as that of claimed SEQ ID NO: 1; the reference peptide FHENWPS comprises the sequence of the claimed

FHENWP of SEQ ID NO: 4 or the claimed peptide HENWPS of SEQ ID NO: 7. As explained earlier, products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure or sequence, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. As such, the intrinsically property of the claimed peptide such as CD23-binding activity as now claimed must present.

The invention in claims 58 and 60 differs from the teachings of the references only in that the peptide has at least one amino acid which is a D-isomer instead of naturally occurring L-isomer.

Heck et al teach in recent years, a growing number of synthetic peptides containing D-amino acids to capitalize on the residues' ability to provide improved protease stability (pharmacokinetic profile) of the bioactive peptides (see page 4039, col. 2, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to improve the stability of the peptide of Jouault et al by substituting the natural occurring L-amino acid in the peptide of Jouault et al for the D-amino acid isomer as taught by Heck et al.

One having ordinary skill in the art would have been motivated to do so because Heck et al teach it is conventional at the time the invention was made to synthesize peptides containing D-amino acids to capitalize on the residues' ability to provide improved protease stability (pharmacokinetic profile), alter tertiary structure and affect activity of the bioactive peptides (see page 4039, col. 2, in particular).

29. Claims 59 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jouault et al (of record, Glycobiology 11(8): 693-701, 2001; PTO 1449) or DE19749277 A1 (of record, published May 5, 1999; PTO 1449) or JP2002187899 (of record, published July 5, 2002 PTO 1449) or Santamaria et al (of record, Clinical Immunology 101(3): 296-302, 2001; PTO 892) each in view of Harlow et al (of record, in Antibodies a Laboratory Manual, 1988, Cold Spring harbor laboratory publication, Cold Spring Harbor, NY, page 321-323, PTO 892).

The teachings of Jouault et al, DE19749277 A1, JP2002187899 and Santamaria et al have been discussed supra. Jouault et al teach the reference peptide mimic epitopes corresponding to small oligomanosides or sugar sequence is highly specific and depends on the

spatial structure presented by the sugar, see page 698, col. 1, in particular). Jouault et al further teaches labeled antibody such as HRP-labeled goat anti-Ig for detection assays (see page 698, col. 2, last paragraph, in particular).

The invention in claim 64 differs from the teachings of the references only in the peptide is further labeled with a detectable marker.

Harlow *et al* teach a method of labeling antibody or antigen (peptide) for a wide range of immunological assays and the advantage of enzyme label such as HRP is the shelf life, high sensitivity, and direct visualization is possible, see page 321-322, Table 9.1, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to label the peptide of Jouault et al, DE19749277 A1, JP2002187899 or Santamaria et al with a detectable label such as Horse radish peroxidase (HRP) for detection or competition assay as taught by Jouault et al or Harlow et al.

One having ordinary skill in the art would have been motivated to label the peptide with any detectable marker such as HRP because the advantage of enzyme label such as HRP is the long shelf life, high sensitivity, and direct visualization is possible as taught by Harlow et al, see page 321-322, Table 9.1, in particular). One having ordinary skill in the art would have been motivated to label the peptide to see if the peptide still binds to the sugar sequence because Jouault et al teach the reference peptide of SEQ ID NO: 1 is a mimic epitope corresponding to small oligomanosides or sugar sequence that is highly specific and depends on the spatial structure presented by the sugar, see page 698, col. 1, in particular). One having ordinary skill in the art would have been motivated to label the peptide because DE19749277 A1 patent teaches the reference peptide also binds to albumin (see abstract, in particular). One having ordinary skill in the art would have been motivated to label the peptide because the JP2002187899 patent teaches the reference peptide has binding affinity to luciferase (see page 11, sequence listing, in particular). One having ordinary skill in the art would have been motivated to label the peptide because Santamaria et al teach peptide is a mimotope of C albincans in patient infected with such (see page 301, col. 1, second paragraph, in particular).

30. No claim is allowed.

31. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

32. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh, Ph.D. whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Thursday from 9:00 a.m. to 6:30 p.m. and alternate Friday from 9: 00 a.m. to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The IFW official Fax number is (571) 273-8300.

33. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phuong Huynh/
Primary Examiner, Art Unit 1644
November 6, 2009